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A prospective study of cigarette tar yield and lung cancer

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We examined the relationship of cigarette tar yield and other cigarette-usage characteristics in current smokers to the incidence of lung cancer in a study population of 79,946 Kaiser Permanente Medical Care Program members, aged 30-89 years, who completed a detailed, self-administered, smoking-habit questionnaire during the years 1979 through 1985. Mean length of follow-up was 5.6 years. There were 302 incident lung cancers, of which 89 percent occurred in current or former smokers. The tar yield of the current cigarette brand was unassociated with lung cancer incidence (relative risk [RR] = 1.02 per 1 mg tar-yield in men, 95 percent confidence interval [CI] = 0.98-1.05; RR = 0.99, CI = 0.96-1.03 in women). However, in long-term (>20 years) smokers, the risk of lung cancer was decreased in women who had smoked filtered cigarettes for 20 or more years relative to lifelong smokers of unfiltered cigarettes (RR = 0.36, CI = 0.18-0.75), but not in men who had smoked filtered cigarettes for 20 or more years (RR = 1.04, CI = 0.58-1.87).

Key words: Cigarettes, lung neoplasms, tars, tobacco smoking, United States.

Introduction

Although many epidemiologic studies have shown that smokers of cigarettes with relatively low yields of tar have a lower risk of lung cancer than smokers of high tar-yield cigarettes, few have examined the relationship of tar yield to lung cancer in a prospective cohort design.[1-4] Two other cohort studies have shown that smoking filtered cigarettes is associated with lower risk of lung cancer than smoking unfiltered cigarettes, presumably because the tar yield of filtered cigarettes is lower.[5,6] Case-control studies also have found a lower risk of lung cancer to be associated with low-tar or filtered cigarette use.[7-11]

In 1979, we began a prospective study of the health effects of smoking low-yield cigarettes in the members of a large, prepaid, health-care program who underwent multiphasic health checkups (MHCs).[15,16] The results of the follow-up through 1987 for lung cancer in this cohort of nearly 80,000 individuals is reported here.

Methods

Study population and follow-up

The study population is composed of 79,946 Kaiser Permanente Medical Care Program members, aged 30-89 (mean age, 48 years), who completed a detailed, self-administered, smoking-habit, research questionnaire in the setting of a multiphasic health checkup (MHC) conducted in the San Francisco (until 1980) and Oakland Kaiser Permanente facilities in California (United States). The study cohort includes those who completed the questionnaire between its inception in mid-1979 through 1985. Follow-up was carried out for lung cancer from the date of the MHC to the date of the

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earliest of the following: diagnosis of lung cancer ($n = 302$); death ($n = 2,275$); membership termination ($n = 15,454$); or 31 December 1987 ($n = 61,915$). The mean length of follow-up was 5.6 years.

Determination of smoking status and of tar content

Persons were classified as current, former, or never-smokers on the basis of their responses to the smoking-habit questionnaire.[17] Current and former smokers also were questioned about: frequency (number of cigarettes per day) and duration (years) of smoking; brand of cigarette usually smoked; characteristics of cigarette brand (length, filtered or unfiltered, mentholated or plain); amount of cigarettes smoked; inhalation habits (frequency and depth of inhalation); and duration (years) of smoking filtered and low-tar cigarettes. The brand of cigarette usually smoked was classified as to tar and nicotine yield according to the Federal Trade Commission Reports.[18-20] The reports of May 1978, March 1981, and March 1983, were used for questionnaires completed before July 1981, July 1981 through December 1983, and January 1984 through December 1985, respectively. The tar yield could not be ascertained for 14 percent of current smokers. The mean tar yield for the brand smoked by current smokers was 14.8 mg.

Source of follow-up data

Determination of lung cancer cases. Incident lung cancers were determined from a summary file of first occurrences of cancer in the Kaiser Permanente Medical Care Program. The main source of cases for this file was the Resource for Cancer Epidemiology, a California state-run and federally supported population-based registry of cancer incidence in the five San Francisco Bay Area counties including Oakland and San Francisco. (The administration changed in 1986 to the Northern California Cancer Center, and the registry is now known as the Bay Area Resource for Cancer Control.) The file also includes cancer cases from the computer-stored records of all overnight hospitalizations in the Northern California Kaiser Permanente Medical Care Program. Cases from the registry were confirmed by registry personnel, while cases determined by hospital discharge diagnosis were confirmed by manual medical-record review.

Mortality. Mortality was ascertained through 1987 by computer-matching the members of the study cohort with the Kaiser Permanente Medical Program membership file as of 1989 and extracting a list of subjects who were no longer members. From this list, we accepted as confirmed deaths, those ascertained in previous studies performed at the Kaiser Permanente Division of Research. The mortality status of the remaining study subjects who were no longer members was ascertained by computer-matching names with the California death file using the California Automated Mortality Linkage and Information System (CAMLIS).[21] Questionable matches were confirmed or excluded by manual record review.

Membership termination data. Annual membership status was determined in June of each year by examination of computerized files. The membership termination date was estimated to be 31 December of the year in which the person last appeared in the June membership file, because that date represents the midpoint between successive June membership updates.

Analytic methods

Statistical analyses were performed using SAS programs.[22] Mantel-Haenzel estimates of the age-adjusted relative risks (RR) of lung cancer associated with current and former smoking were obtained.[23] For each individual, person-years of follow-up were assigned to appropriate age categories using attained age for the duration of follow-up. Incidence rates were age-adjusted by the direct method using the age distribution of current smokers as the standard. Cox proportional hazards models were used to examine the joint effect of multiple sociodemographic and smoking characteristics on the risk of lung cancer.[24] RRs associated with tar yield and selected cigarette-usage characteristics in current smokers were obtained by entering each of these characteristics individually in a proportional hazards model which included age, gender, race, and education, as well as the frequency and duration of smoking.

Results

The prevalence of current smoking was related inversely to age, and was higher in men than in women (Table 1). Among the race categories in this study, the prevalence of smoking was highest in Blacks, followed by Whites, and lowest in Asians. Graduation from college was associated with a lower prevalence of smoking than lesser degrees of education.

There were 302 incident lung cancers in this cohort through 1987, of which 89 percent were in current or former smokers. Age-specific RRs for lung cancer ranged from 11.3 to 34.9 for current smokers (*cf* nonsmokers) (Table 2); the age-adjusted RR of lung cancer for current smokers was 12.8 (95 percent confidence

Table 1. Distribution of cigarette smoking status by age, gender, race, and education (No., with % in parentheses)

	Nonsmoker	Former	Current	Total
Age				
30-49	23,080 (49)	9,457 (20)	14,857 (31)	47,394
50-64	11,156 (48)	5,748 (25)	6,152 (27)	23,056
65-74	4,032 (55)	1,902 (26)	1,391 (19)	7,325
75-89	1,551 (71)	434 (20)	186 (9)	2,171
Gender				
Men	14,413 (41)	9,822 (28)	10,740 (31)	34,975
Women	25,406 (57)	7,719 (17)	11,846 (26)	44,971
Race				
White	21,761 (47)	12,247 (27)	12,212 (26)	46,220
Black	8,986 (45)	3,382 (17)	7,461 (38)	19,829
Asian	6,385 (72)	1,052 (12)	1,454 (16)	8,891
Other/unknown	2,687 (54)	860 (17)	1,459 (29)	5,006
Education				
≤ High school	10,327 (48)	4,085 (19)	6,999 (33)	21,411
Technical/business	2,447 (47)	1,193 (23)	1,552 (30)	5,192
Part college	8,477 (44)	4,384 (23)	6,530 (34)	19,391
College graduate/post	15,878 (54)	7,087 (24)	6,495 (22)	29,460
Unknown	2,690 (60)	792 (18)	1,010 (22)	4,492
Total	39,819 (50)	17,541 (22)	22,586 (28)	79,946

interval [CI] = 8.7-18.7). Age-specific RRs for lung cancer ranged from 4.5 to 7.0 for former smokers; the age-adjusted RR of lung cancer for former smokers was 5.5 (CI = 3.7-8.2).

Frequency and duration of cigarette smoking were related strongly to the incidence of lung cancer in smokers. An increase in smoking frequency of 10 cigarettes per day was associated with a 33 percent increase in the risk of lung cancer ($P < 0.0001$), adjusted for age, gender, race, education, and duration of smoking. A 10-year increase in duration of smoking was associated with a 63 percent increase in the risk of lung cancer ($P < 0.0001$), adjusted for frequency of smoking and the sociodemographic variables. The vast majority of lung cancers were associated with a history of at least 20 years of smoking. The risk of lung cancer in former smokers diminished with increasing length of time since quitting, but was still nearly twice that of nonsmokers in those who quit 15 or more years before the MHC (RR = 1.9, CI = 1.1-3.5).

The RR of lung cancer in current smokers associated with selected cigarette-usage characteristics is shown in Table 3, adjusted for age, race, education, frequency of smoking (cigarettes/day), and duration of smoking (years). The cut-points for tar yield were chosen so that approximately 25 percent of smokers would be in the highest and the lowest categories. Tar content was not significantly associated with the risk of lung cancer in either men or women. Frequency of inhalation (all or most times *cf* other categories) was associated with increased risk of lung cancer in women only (RR = 2.1, $P = 0.02$). None of the remaining characteristics was associated significantly ($P < 0.05$) with lung cancer in either men or women. These associations did not change substantially in analyses limited to longer-term smokers, *i.e.*, those with a history of at least 20 years of

Table 2. Incidence of lung cancer by age and smoking status, and relative risk (RR) and 95% confidence interval (CI) of lung cancer in current and former smokers compared with nonsmokers

Age group	Current		Former		Never		Current		Former	
	No. of events	Rate/ 100,000	No. of events	Rate 100,000	No. of events	Rate/ 100,000	RR	(CI)	RR	(CI)
30-49	22	32.7	2	4.8	1	0.9	34.9	(4.7-258.9)	5.1	(0.5-56.7)
50-64	89	224.8	37	110.0	13	19.1	11.8	(6.6-21.1)	5.8	(3.1-10.9)
65-74	54	406.5	27	161.8	12	36.0	11.3	(6.0-21.1)	4.5	(2.3-8.9)
75-89	19	671.3	18	341.6	8	48.5	13.8	(6.1-31.6)	7.0	(3.1-16.2)

Table 3. Incidence and relative risk (RR) and 95% confidence interval (CI) of lung cancer associated with selected cigarette use characteristics in current smokers

Characteristic	Men				Women			
	No. cases	Rate[a] (per 100,000 person-years)	RR[b]	(CI)	No. cases	Rate[a] (per 100,000 person-years)	RR[b]	(CI)
Frequency of inhalation								
All or most of time	76	143.5	1.12	(0.66-1.89)	63	122.1	2.05	(1.12-3.74)
Other (reference)	20	91.4	—		17	60.8	—	
Depth of inhalation								
Deep	25	203.5	1.44	(0.89-2.34)	6	85.3	0.74	(0.32-1.73)
Other (reference)	71	115.5	—		74	100.3	—	
Amount of cigarettes								
> 3/4 pack	37	132.9	0.98	(0.64-1.50)	29	105.7	1.10	(0.68-1.79)
≤ 3/4 pack (reference)	58	127.2	—		50	91.4	—	
Filter								
Yes	81	135.6	1.03	(0.61-1.75)	74	95.2	0.65	(0.32-1.31)
No (reference)	17	118.0	—		9	217.2	—	
Tar								
< 11 (reference)	14	107.0	—		29	128.5	—	
11-18	39	136.5	1.29	(0.69-2.43)	34	102.7	0.93	(0.55-1.59)
> 18	29	116.9	1.27	(0.67-2.43)	13	86.0	0.67	(0.34-1.32)
Tar (continuous)	N/A	N/A	1.02	(0.98-1.05)	N/A	N/A	0.99	(0.96-1.03)

[a] Age-adjusted rate, adjusted by direct method using the age distribution of current smokers as the standard.
[b] Adjusted for age, race, education, cigarettes/day, and number of years of smoking.

smoking. Though age and duration of smoking were highly correlated (correlation coefficients = 0.77 for men and 0.73 for women), each was associated significantly with lung cancer in the multivariate model, and the relationship of other cigarette-usage characteristics to lung cancer risk was not altered appreciably by the removal of either age or duration of use from the model.

We did not collect historical information about all brands smoked, so we could not ascertain a long-term history of tar yields in brands used by smokers. In order to examine indirectly the relationship of low-yield cigarette use to lung cancer, we examined the relationship of self-reported duration of filtered and of low-tar cigarette smoking to lung cancer incidence in current smokers with a history of at least 20 years of smoking. Duration of filtered cigarette use was related inversely to the risk of lung cancer in women only, adjusted for age, race, education, frequency, and duration of smoking (Table 4). These associations did not change significantly when the proportion of smoking-lifetime, represented by duration of filtered cigarette use, was substituted for years of filtered cigarette use, nor were they altered when the cigarette usage characteristics were entered individually as independent variables into the statistical models. There was a 64 percent decrease in the risk of lung cancer in women who smoked filtered cigarettes for 20 years or longer relative to the risk in women who were lifetime smokers of unfiltered cigarettes. Duration of low-tar cigarette use was unrelated to lung cancer.

Discussion

The tar yield of current cigarettes was unassociated with lung cancer in this study. Other studies which

Table 4. Relative risk (RR) and 95% confidence interval (CI) of lung cancer associated with duration of filtered cigarette use in current smokers with a history of at least 20 years of smoking (12,038 observations; 166 cases)

Duration of filtered cigarette use (years)	Men			Women		
	No. cases	RR[a]	(CI)	No. cases	RR[a]	(CI)
0 (reference)	16	1.0		10	1.0	
1-9	7	0.72	(0.30-1.76)	10	1.08	(0.45-2.59)
10-19	27	0.93	(0.50-1.75)	22	0.70	(0.33-1.49)
≥ 20	43	1.04	(0.58-1.87)	31	0.36	(0.18-0.75)

[a] Adjusted for age, race, education, cigarettes/day, and number of years of smoking.

Table 5. Cohort and case-control studies regarding the relationship of cigarette tar yield or of filtered cigarette use to lung cancer[a]

Author	(Ref#)	Cohort studies				
		Location of study	Size of cohort	Length of follow-up	No. of lung cancers	Results
Hammond	(1)	USA	458,573 men 593,665 women	2 6-year follow-up periods	839 "adjusted" deaths in smokers	Mortality ratios for lung cancer in smokers associated with low yield cigarettes (< 1.2 mg nicotine, < 17.6 mg tar [with rare exception for tar cutoff]) relative to high yield cigarettes (≥ 2.0 mg nicotine, ≥ 25.8 mg tar) during two 6-year follow-up periods were 0.83 and 0.79 for men, and 0.57 and 0.62 for women. Mortality ratios for lung cancers in smokers associated with intermediate yield cigarettes relative to high yield cigarettes were 0.96 and 0.94 for men, and 0.86 and 0.73 for women
Steilman	(2)	USA	222,830 White men	6 years	969	Standardized mortality ratio (SMR) for lung cancer in smokers associated with low tar cigarette (≤ 17.6 mg) use was 32% lower than the SMR associated with high tar cigarette (≥ 25.7 mg) use
Garfinkel	(3)	USA	619,925 women	4 years	1,006	A 5 mg increase in cigarette tar yield was associated with a 17% increase in risk of lung cancer mortality in current smokers. The standardized mortality for women who smoked filters for 40% of their smoking lifetime or less was 1.51 (1. 29, 1.75) compared with women who smoked filter cigarettes only, among current smokers who had smoked for at least 20 years
Higgenbottom	(4)	UK	17,475 men	10 years	193	Mortality rate for lung cancer associated with tar yield ≥ 33 mg/ cigarette was compared with that of smokers of cigarettes with 18-23 mg tar. Results were inconsistent across categories of cigarettes smoked per day
Hawthorne	(5)	Scotland	11,295 men	2-12 years	104	Risk of lung cancer in male current smokers was 17% lower (not statistically significant) in those who normally smoked filtered cigarettes relative to those who normally smoked plain cigarettes
Rimington	(6)	England	10,414 men	69-81 months	104	Risk of lung cancer associated with filter cigarette use relative to non-filter cigarette use was 0.65

Continued ...

Table 5. *Continued*

Author	(Ref#)	Case-control studies			
		Location of study	No. of cases	No. and type of controls	Results
Lubin	(7)	Western Europe	6,920 men 884 women	13,460 men 1,747 women hospital-based	Risk of lung cancer associated with lifetime filter cigarettes relative to lifetime nonfilter cigarette use was 1.7 for men and 2.0 for women. Non-graded increased risk of lung cancer with increased tar
Wilcox	(8)	New Jersey (USA)	727 men	671 men population-based	Risk of lung cancer associated with tar yield ≤ 14 mg/cigarettes relative to tar yield 21.1-28 mg/cigarettes was 0.6 (95% confidence interval 0.3, 1.1)
Kaufman	(9)	USA and Canada	534 men 347 women	998 men 1,572 women hospital-based	Risk of lung cancer associated with tar yield ≥ 29 mg/cigarette relative to tar yield < 22 mg/cigarette was 4.0 (1.2, 13) for men and 4.7 (1.1, 21) for women for cigarettes smoked at least 10 years before admission
Bross	(10)	Buffalo, NY (USA)	974 White men	974 White men hospital-based	Risk of lung cancer associated with current use of filtered cigarettes relative to use of regular cigarettes was 0.59 (crude); risk associated with filtered cigarette use was generally lower relative to regular cigarette use in 9 different strata of duration and frequency of use
Dean	(11)	England	616 men 150 women	2,563 men 2,958 women population-based	Risk of lung cancer deaths associated with use of mainly filtered cigarettes relative to mainly plain cigarettes was 0.41
Wynder	(12)	USA	557 men 127 women	4,835 men 4,712 women hospital-based	Risk of lung cancer associated with cigarette use ≥ 10 years in current nonfilter smokers relative to long-term filter smokers was 1.26 (0.97, 1.64) in men and 1.37 (0.72, 2.60) in women
Benhamou	(13)	France	1,217 men	1,915 men hospital-based	Risk of lung cancer associated with nonfilter cigarette use relative to lifetime filter cigarette use was 1.23 for current and former smokers combined (not statistically significant)
Wynder	(14)	USA	2,087 men 1,012 women	3,951 men 1,892 women hospital-based	Risk in current smokers of ≥ 10 years duration lifetime filter only use relative to nonfilter only use was 0.69 (0.37, 1.27) in men and 0.64 (0.30, 1.35) in women for Kreyberg I lung cancer (squamous cell, large cell, and oat cell) and was 0.87 (0.43, 1.54) in men and 0.96 (0.62, 1.47) in women for Kreyberg II lung cancer (adenocarcinoma, bronchial, and alveolar cell carcinoma)

[a] Results generally are adjusted for age or duration of smoking, and for number of cigarettes smoked per day; in some cases, adjustment is made for other characteristics.

have examined the relationship of tar yield or filtered cigarette use to lung cancer are summarized in Table 5. The American Cancer Society's (ACS) Cancer Prevention Studies (I and II) and the Whitehall Study are the only other prospective cohort studies of which we are aware that have examined the relationship between tar yield and lung cancer.[1-4] In the Cancer Prevention Study I, low tar (≤ 17.6 mg) cigarettes were associated with lower mortality from lung cancer than medium (17.7-25.6 mg) and high tar (> 25.6 mg) cigarettes.[1,2] Lung cancer risk in women increased about 40 percent with a doubling of tar yield in the ACS Cancer Prevention Study II, in which nearly all cigarettes smoked by women had tar yields ≤ 20.2 mg.[3] In the Whitehall Study, tar yield was associated with lung cancer mortality in smokers of less than one pack per day who inhaled, and in smokers of one-half pack or more per day who did not inhale.[4] Tar yield was related to lung cancer risk in three case-control studies.[7-9] Studies of the relationship of tar yield to lung cancer have been inconsistent in their controlling for the effects of frequency of smoking.

Possible reasons for the negative findings regarding the relationship of tar yield to lung cancer in this study include compensatory efforts by smokers of low yield cigarettes to increase yield by more vigorous inhalation patterns or by smoking more cigarettes; the latter has been demonstrated previously in this cohort.[25] However, the results were not changed substantially when adjustment for these variables was performed. The inability to assess the long-term tar exposure in our study is a limitation. The tar yield of cigarettes smoked by an individual was likely to have changed over time due to secular trends which have resulted in lower yields from cigarettes in general,[26] and due to brand changes made by the individual. We had available only a relatively late assessment of tar intake. This is an especially important consideration since smoking habits early in life are related strongly to the risk of lung cancer later in life.[27] Another factor which may have an impact on the results of this study is the relatively low level of the cigarette tar yields relative to nearly all the studies reviewed, with the exception of the studies of Garfinkel *et al*[5] and Wilcox *et al*.[8] Lack of statistical power is an unlikely explanation for the negative findings in regard to tar yield, since there was no suggestion of any association between tar content and lung cancer incidence.

The finding of an inverse association between lung cancer risk and filtered cigarette use in women who were long-term smokers is consistent with other cohort[4,5] and case-control[7,12,13] studies. The magnitude of this association is larger in this study than in the other studies. It is likely that the lack of an association between lung cancer risk and filtered cigarette use in men is due to chance. The CI around the estimate of RR associated with the categories of duration of filtered cigarette use was wide and included the estimate of the RR noted in almost all the studies (except for Dean *et al*[11]) which examined the relationship of filtered cigarette use to lung cancer. The results in this and other studies may be biased by unmeasured potential confounders, such as dietary factors and occupational exposures. This study and most other studies of the association of low tar and/or filtered cigarette use with lung cancer have shown more benefit in lowering lung cancer risk associated with the use of filtered cigarettes in women than in men, suggesting the possibility that biologic factors or unmeasured aspects of the smoking habit which differ by gender may influence the impact of filtered cigarette use or of changing tar yield on lung cancer risk.

The association of frequency of inhalation with lung cancer in women is plausible, in that the intake of various components of cigarette smoke depends not only on the number of cigarettes smoked but on patterns of inhalation and puffing. Frequency of inhalation and/or depth of inhalation have been associated with lung cancer in other studies.[3,7,13] The strength of the relationship of frequency and of duration of smoking to lung cancer are consistent with the findings of other studies, as is the relationship between the length of time since quitting to lung cancer in former smokers.[28]

In summary, there was no association between the tar yield of the currently used cigarette-brand and the risk of lung cancer in this study. Duration of filtered cigarette use in long-term smokers was associated inversely with the risk of lung cancer in women, but not in men. It is important to place this finding in the context that smoking any kind of tobacco cigarette is strongly related to lung cancer, and that frequency and duration of cigarette smoking are more important risk factors for lung cancer than differences in the physical characteristics and biochemical composition of cigarette brands.

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